Palladium(II) Catalyzed Carboxylation of Aromatic Compounds with CO under Very Mild Conditions

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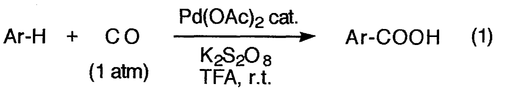
(Received January 30, 1995)

Aromatic compounds in trifluoroacetic acid were readily carboxylated with CO in the presence of a catalytic amount of palladium(II) acetate under mild conditions to give aromatic carboxylic acids in good yields.

In previous papers, we reported direct carboxylation of aromatic compounds with CO or CO_2 by palladium catalysts.[1] However, the reaction requires severe reaction conditions such as high CO pressure and temperatures. In the course of a survey of the synthetic reactions *via* the transition metal catalyzed C-H bond activation, we found that the $Pd(OAc)_2/K_2S_2O_8$/trifluoroacetic acid (TFA) system[2] caused the direct carboxylation of arenes under very mild reaction conditions. We now wish to report the details of the reaction as depicted in eq. 1.



$$\text{Ar-H} + \underset{(1\text{ atm})}{\text{CO}} \xrightarrow[\substack{K_2S_2O_8 \\ \text{TFA, r.t.}}]{Pd(OAc)_2\text{ cat.}} \text{Ar-COOH} \quad (1)$$

First, we examined the carboxylation reaction of benzene to give benzoic acid (**1**) using benzene (5 mL, 56 mmol) and CO (1 atm) in the presence of $Pd(OAc)_2$ (0.5 mmol), and an oxidizing agent in TFA (5 mL) at room temperature for 20 h. These results are listed in Table 1. In the absence of an oxidizing agent, reaction gave **1** in 23% yield, and palladium black precipitated as the reaction proceeded (entry 1 in Table 1). Addition of $Cu(OAc)_2$ increased the yield of **1** although the reaction did not proceed catalytically (entries 1 and 2 in Table 1). In order to make the reaction catalytic with respect to palladium(II), several oxidizing agents of Pd(0) to Pd(II) were tested. Of the oxidizing agents, $K_2S_2O_8$ in TFA was found to give the best result (entry 4 in Table 1). In the $Pd(II)/K_2S_2O_8$ catalytic system, the addition of $Cu(OAc)_2$ decreased the yield of **1** in contrast to the reactions without $K_2S_2O_8$.

Table 1. $Pd(OAc)_2$ Catalyzed Direct Carboxylation of Benzene[a]

Entry	Oxidizing Agent (5 mmol)	$Cu(OAc)_2$ (mmol)	Yield of **1** (%)[b]
1	none	none	23
2	none	0.5	72
3	none	0.5	0[c]
4	$K_2S_2O_8$	none	570
5	$K_2S_2O_8$	5.0	84
6	*tert*-BuOOH	none	trace
7	Oxone[d]	none	-[e]

[a] $Pd(OAc)_2$ (0.5 mmol), benzene (5 mL), oxidizing agent (5 mmol), TFA (5 mL), CO (1 atm), r.t., 20 h. [b] Isolated yield based on Pd. [c] No Pd(II) salt was used. [d] $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$. [e] Complex reaction occurred.

Then, the effect of the amount of $Pd(OAc)_2$ on the yield of **1** under similar reaction conditions was investigated. These results are shown in Figure 1. As is apparent from Figure 1, the yields of **1** increased with decreasing amounts of $Pd(OAc)_2$. It seems that the yield of the carboxylation of benzene does not depend on the amounts of $K_2S_2O_8$ but does on the amount of $Pd(OAc)_2$.

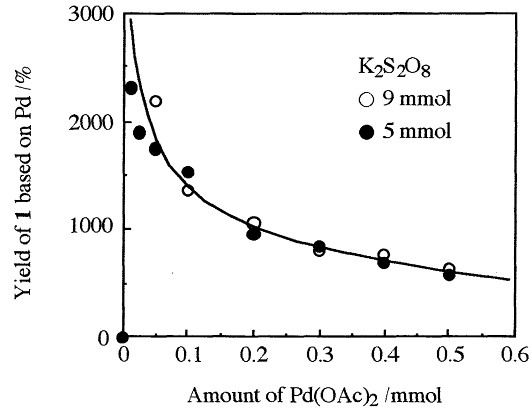


Figure 1. Relationship of $[Pd(OAc)_2]$ vs. yield of **1**.

The representative results for the palladium(II)-catalyzed carboxylation of various aromatic compounds under mormal CO pressure and at room temperature are summarized in Table 2. Various aromatics are converted to the corresponding aromatic carboxylic acids in good yields under mild conditions (entries 6-9 in Table 2). Entries 1-5 in Table 2 indicate the time course of the carboxylation of benzene. The yield of **1** increased monotonously, and after 120 h the yield became almost constant. Toluene, anisole, and chlorobenzene gave the corresponding acids with *ortho-para* orientation, and naphthalene afforded α- and β-naphthoic acids in a 66:34 ratio.

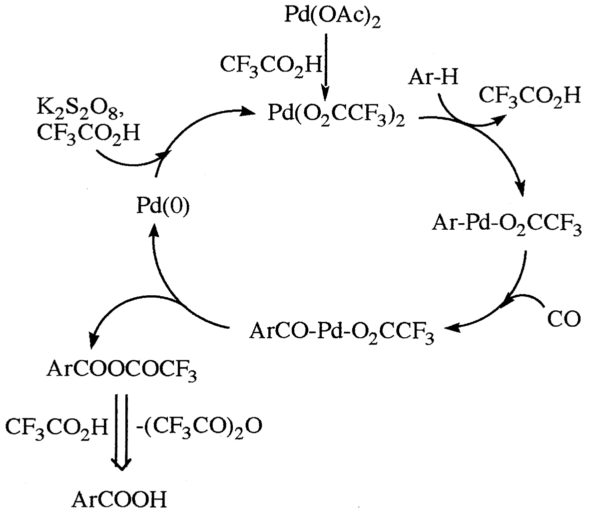
The typical preparation of **1** is as follows (entry 5 in Table 2): a solution of $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), benzene (5 mL, 56 mmol) and $K_2S_2O_8$ (1.352 g, 5 mmol) in TFA (5 mL) was placed in a 50 mL round-bottomed flask equipped with a baloon filled with CO. The mixture was stirred at room temperature for 120 h. Usual work-up gave **1** (397 mg) in 3300% yield based on Pd.

That the reaction proceeds with *ortho-para* orientation when an electron-releasing group is attached to the benzene ring and that naphthalene gives α-naphthoic acid as a main product suggest that the reaction proceeds *via* electrophilic attack of cationic palladium(II).[3] Competitive reaction of benzene and chlorobenzene with CO gave benzoic and chlorobenzoic acids in 580 and 60% yields, respectively. The relative reactivity was found to be in the order of anisole > toluene > benzene > chloro-

Table 2. $Pd(OAc)_2$ Catalyzed Direct Carboxylation of Arenes[a]

Entry	Substrate	Time (h)	Product	Yield[b]
1	Benzene	5	Benzoic acid (**1**)	600
2	"	10	"	800
3	"	20	"	1400
4	"	40	"	2200
5	"	120	"	3300
6	Toluene	20	Toluic acids	800[c] (26:6:67)[d]
7	Chlorobenzene	20	Chlorobenzoic acids	1700 (19:27:54)[e]
8	Anisole	20	Anisic acids	1200[c] (33:0:67)[d]
9	Naphthalene	20	Naphthoic acids	3300 (66:34)[f]

[a] $Pd(OAc)_2$ (0.1mmol), arene (56 mmol), CO (1 atm, baloon), $K_2S_2O_8$ (5 mmol), TFA (5 mL), r.t.. [b] Isolated yield based on Pd. [c] Coupling products were also formed in considerable amounts. [d] *o*:*m*:*p*-Isomer ratio was determined by ^{13}C NMR. [e] *o*:*m*:*p* -Isomer ratio was determined by GLC analysis of the methyl esters. [f] α,β-Isomer ratio was determined by GLC analysis.



Scheme 1. Possible Mechanism for Palladium(II)-Catalyzed Direct Carboxylation of Arenes.

benzene by competitive reactions. This result also indicates that the reaction is electrophilic.

In order to increase the conversion of benzene for the synthesis of **1**, the effect of the amounts of benzene, $K_2S_2O_8$, and TFA was tested. These results are listed in Table 3. One can see that the yield of **1** increases with decreasing amounts of benzene and TFA. The datum of entry 5 in the table shows that the carboxylation of benzene proceeds quantitatively when 1 mmol of benzene, 2.5 mmol of $K_2S_2O_8$, and 1 mL of TFA were employed in the presence of 10 mol% of $Pd(OAc)_2$ catalyst. Under those optimum conditions, the carboxylations of chlorobenzene, toluene and anisole proceeded to afford the corresponding acids in 100; 67, and 60% yields besed on substrate, respectively.

Table 3. Effect of the Amounts of Benzene, $K_2S_2O_8$, and TFA[a]

Entry	Benzene (mmol)	$K_2S_2O_8$ (mmol)	TFA (mL)	Yield of **1** (%)[b]	
1	56	5	5	2.5	(1400)
2	10	5	5	17	(1700)
3	1	2.5	5	48	(480)
4	1	2.5	2.5	89	(890)
5	1	2.5	1	100	(1000)

[a] $Pd(OAc)_2$ (0.1mmol), CO (1 atm, baloon), r.t.. [b] Isolated yields based on benzene and the numbers in parentheses are the yields based on Pd.

Isotope effect for this carboxylation process was examined by using d_6-benzene. The competitive reaction of C_6H_6 and C_6D_6 with CO afforded the mixture of **1** and d_5-**1**. The k_H/k_D ratio was found to be 6.1 by GC-MS analysis of the products. This result indicates that the rate-determining step of this reaction is the C-H bond activation of arenes.

Possible reaction mechanism is shown in Scheme 1. Electrophilic attack of an electropositive $Pd^+(OCOCF_3)$ species on the benzene ring gives an arylpalladium species, which undergoes insertion of CO to give an aroylpalladium(II). The subsequent reductive elimination gives palladium(0) and the acid anhydride which react with TFA to give ArCOOH and $(CF_3CO)_2O$. Palladium(0) is reoxidized by $K_2S_2O_8$ to Pd(II). The reason why the present reaction proceeds under the milder conditions than those of the usual $Pd(OAc)_2$/AcOH system[1], could be attributed to the formation of more electropositive $Pd^+(OCOCF_3)$ as compared with $Pd^+(OCOCH_3)$ which is formed under the usual conditions.

We are grateful for grants from Idemitsu Petrochemical Co., Ltd., Daicel Chemical Co., Ltd, and Sumitomo Chemical Ind., Ltd.

References and Notes

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